REMARKS

The present response relates to the Office Action in the above-identified application mailed on August 23, 2004. Claims 1-22 are pending. Claims 1-13 are rejected. Applicant previously cancelled Claims 14-22 due to an election/restriction requirement. Applicant amends Claims 1, 5-8 and 11-2, cancels Claim 9 and adds new Claims 23-32. No new matter is presented by these amendment. Applicant respectfully requests reconsideration and favorable action in this case.

Rejections under 35 U.S.C. § 112

Claims 1 and 9 were rejected by the Examiner under 35 U.S.C. §112, first paragraph, for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the application was filed, had possession of the claimed invention. Applicant amends Claim 1 and cancels Claim 9 to overcome these rejections and respectfully request full allowance of Claim 1 as amended. Specifically, Claim 1 has been amended to recite a GAL4 common peptide.

Rejections under 35 U.S.C. § 102

Thukral

Claims 1-4, 10, 11 and 13 were rejected by the Examiner under 35 U.S.C. § 102 (a) and 102(e) as being anticipated by U.S. Patent 6,103,472 issued to Sushil K. Thukral ("Thukral"). Claim 1 (and hence dependent Claims 2-4, 10, 11 and 13,) is not anticipated by Thukral, as explained in the present application at page 6, paragraph 13 and in Thukral itself relates to methods of detecting protein secretion signal sequences (Col. 1, lines 6-7; Col. 2, lines 35-39; Col. 3, lines 51-55). Because of this stated goal, Thukral only discloses the use of common peptide reporter sequences that "confer a property or activity when secreted which may be readily assayed" (Col. 3, lines 55-61). Thus Thukral does not relate to assays, such as yeast two-hybrid assays, that are performed inside a cell. Claims 1 as amended relates to plasmids functional in yeast two-hybrid assays using a GAL4 common peptide; it does not relate to assays for detecting secretion of a protein. In fact, secretion of a protein would significantly hamper any two-hybrid assay and most likely prevent the detection of any positive interaction by that method entirely.

Further it is not clear whether or not the plasmids of Thukral contain an independent translational start sequence, or rely upon the translational start sequence in the encoded protein. Although Thukral does disclose example fusion proteins containing the initial Met of signal sequence-containing peptides (Example 2, particularly Table 1), it is not clear if translation of these proteins is initiated by the DNA encoding the fusion protein, or an earlier initiation sequence located 5' to the multiple cloning site. Although the DNA encoding the fusion protein as disclosed in Thukral most likely could initiate its own translation, this is not necessarily the case.

Further, the plasmid used as the basis for the signal trap plasmids disclosed in Thukral provides further evidence that a translation initiation sequence other than that in the DNA inserted at the muliple cloning site might have been used. Thukral fails to provide any sequence information for the two plasmids disclosed therein, pYYA-41L and pYYA-2. Applicant's further exploration of the art has not yielded any other information about either plasmid that would indicate the presence or absence of a translation initiation codon outside of the multiple cloning site in either plasmid.

However, as Example 1 of Thukral describes, these plasmids appear to have been derived from Clontech's pGBT9 plasmid (Col. 10, line 33). pGBT9 is described on Clontech's web page as containing the GAL4 translation initiation sequence before its multiple cloning site. It does not appear from the description in Thukral's Example 1 that this translation initiation codon was removed during the creation of YYA-41L or pYYA-2. In fact, there is no reason for Thukral to have removed the translation initiation codon. Thukral was interested in the amino end of proteins because of secretion signals. Thukral did not need the inserted DNA to include the translation initiation codon, as this is not a part of all secretion signals. In fact, reliance upon the inserted DNA's own translation initiation codon might cause the invention of Thukral to miss some secretion signals if the insert contained nearly, but not all of the amino terminus coding region. Thus, there is ample reason for Thukral to have used the pGBT9 translation initiation sequence rather than to have relied upon such a sequence in the inserted DNA.

In summary, Thukral does not explicitly disclose a plasmid vector lacking a translation initiation sequence other than that in a cDNA inserted at the multiple cloning site. Further, Thukral does not inherently disclose such an a plasmid vector because it does not necessarily use such a vector. Thukral does not discuss translation initiation codons explicitly anywhere in the patent. Thukral discusses only two specific plasmids within the

scope of that invention. Those plasmids are not described with sufficient specificity in the application or, to Applicant's knowledge, elsewhere for one to know whether they contain a separate translation initiation codon. However, based on the plasmid from which they are derived and the goals of Thukral, there is reason to suspect that they do. In any event, the plasmids of Thukral do not necessarily lack a translation initiation codon other than that in the cDNA insert, as claimed in present Claim 1. Thus Thukral also fails to inherently disclose the claimed subject matter.

Finally, Thukral does not disclose a cDNA insert population generated using random primers and hence enriched in its representation of the 5' region of genes as compared to those generated using poly T. Claim 1, as amended, specifically claims a 5' enriched population, which results from use of random primers. This is a physical characteristic of the cDNA insert population and thus is a structural limitation with patentable weight. Thukral does not disclose any methodologies capable of generating such a cDNA population or its use.

Although Claims 25 and 32 are new and thus have not been rejected in light of Thukral, Applicants note that many arguments made above with respect to Claim 1 may also be applicable to differences between Claims 25 and 32 and Thukral.

Fields

Claims 1-3 were rejected by the Examiner under 35 U.S.C. § 102 (b) as being anticipated by U.S. Patent 5,468,614 issued to Stanley Fields et al. ("Fields et al."). Fields discloses a yeast two-hybrid system. As described above, Claim 1 has been amended to specifically indicate that the cDNA insert population is enriched in its representation of the '5 ends of genes. This results from the use of random primers rather than the traditional polyT primer in generating cDNA. Fields does not disclose the use of random primers or any other techniques that result in a 5' end enrichment. Fields further does not disclose any 5' enriched populations. The 5' enrichment of the cDNA population claimed in Claim 1 is a physical characteristic and thus a structural element with patentable weight.

Although Claims 25 and 32 are new and have not been rejected in light of Fields, Applicants not that these claims also recite a 5' enriched cDNA population and thus are not anticipated for the reasons expressed above.

Accordingly, Applicants believe that Claim 1 and hence all dependent claims are not anticipated by either Thukral or Fields.

Rejections under 35 U.S.C. § 103

Claims 4 and 10-13 were rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Fields in view of Thukral. As discussed above, neither Thukral nor Fields disclose all of the elements of Claim 1 (and hence its dependent claims). Nor do Thukral or Fields, alone or in combination, teach or suggest all of the elements of Claim 1. Specifically, with respect to Claim 4, which is now incorporated in Claim 1, the Examiner stated that it would have been obvious to combine the teaching of Thukral and Fields to arrive at a vector with the elements of Fields and a separate 3' translation termination sequence. However, Applications submit that, even if such a combination would provide all of the elements of Claim 1, one skilled in the art would not combine Thukral and Fields. Specifically, the Examiner has correctly identified Fields as a yeast-two hybrid system patent. However, the Examiner appears to have overlooked the nature of the Thukral patent. As explained above, Thukral relates to secreted proteins. The secretion of either the bait or the prey protein would seriously hamper, if not prevent, the function of such protein in a two-hybrid assay. Thus, as a general matter, one would not expect the secretion-related constructs of Thukral to be useful in the two-hybrid assay of Fields.

Additionally, both the disclosure of Fields and that of Thukral lack any teaching or suggestion to use a cDNA population enhanced for 5' ends. Although both might benefit from this, neither reference appears to have developed a way to achieve enhanced 5' representation. Applicants have invented, *inter alia*, a method of increasing the representation of the 5' ends of genes in the cDNA insert population by using random primers to create the cDNA. This enriched population, as claimed in Claim 1, is a physical characteristic of the cDNA and thus has patentable weight. Neither Thukral nor Fields discuss any such enriched population. This absence, particularly when one considers that both inventions may have benefited from it, indicates that neither reference contemplated an enriched population. Thus, the recited combination does not teach or suggest the invention of Claims 4 and 10-13, which are dependent upon Claim 1.

Claim 5 was rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Fields or Thukral, each in view of U.S. Patent 5,679,647 issued to Dennis A. Carson et al. ("Carson et al.). Neither Thukral nor Fields, as discussed above, disclose a 5' enriched cDNA insert population. Carson does not remedy this deficiency. Accordingly, the recited

combinations do not teach or suggest the invention of Claim 5, which is dependent upon Claim 1.

Claim 6 was rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Fields or Thukral, each in view of Bertrand Le Douarin et al., "A New Version of the Two-Hybrid Assay for Detection of Protein-Protein Interactions", vol. 23, pages 876-878, 1995 ("Le Douarin et al."). Neither Thukral nor Fields, as discussed above, disclose a 5' enriched cDNA insert population. LeDouarin does not remedy this deficiency. Accordingly, the recited combinations do not teach or suggest the invention of Claim 6, which is dependent upon Claim 1.

Claim 7 was rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Fields in view of U.S. Patent 6,329,209 issued to Peter Wagner et al. ("Wagner et al.). Neither Thukral nor Fields, as discussed above, disclose a 5' enriched cDNA insert population. Wagner does not remedy this deficiency. Accordingly, the recited combinations do not teach or suggest the invention of Claim 7, which is dependent upon Claim 1.

Claim 8 was rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Fields in view of U.S. Patent 5,679,566 issued to Feng He et al. ("He et al.). Neither Thukral nor Fields, as discussed above, disclose a 5' enriched cDNA insert population. He does not remedy this deficiency. Accordingly, the recited combinations do not teach or suggest the invention of Claim 8, which is dependent upon Claim 1.

Claim 12 was rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Thukral. Thukral, as discussed above, disclose a 5' enriched cDNA insert population. Accordingly, is does not teach or suggest the invention of Claim 13, which is dependent upon Claim 1.

Although Claims 25 and 32 are new and have not been rejected in light of Fields, Applicants these claims also recite a 5' enriched cDNA population and thus are not obvious for the reasons presented above.

Information Disclosure Statement

Applicant encloses an Information Disclosure Statement for the Examiner's review and consideration along with a check in the amount of $180.00

CONCLUSION

Applicant believes Claims 1-32 are now in condition for allowance.

Applicant believes a fee of $225.00 is due at this time for a two-month extension of time for a small entity, which is requested. A check is enclosed in this amount. Should any additional fees be due as a result of this amendment or for any other reason during prosecution of this application, the Commissioner is hereby authorized to charge the payment of any required fees to Deposit Account No. 50-2148.

Respectfully submitted,

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